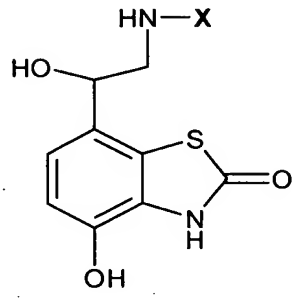
Amendments to the Claims

Listing of Claims:

CLAIMS

Claims 1-20 (canceled)

Claim 21 (new): A medicament comprising, separately or together
(A) a compound of formula I



I

in free or salt or solvate form, wherein

X is $-R^1-Ar-R^2$ or $-R^a-Y$;

Ar denotes a phenylene group optionally substituted by halo, hydroxy, C_1-C_{10}-alkyl, C_1-C_{10}-alkoxy, C_1-C_{10}-alkoxy-C_1-C_{10}-alkyl, phenyl, C_1-C_{10}-alkyl substituted by phenyl, C_1-C_{10}-alkoxy substituted by phenyl, C_1-C_{10}-alkyl-substituted phenyl or by C_1-C_{10}-alkoxy-substituted phenyl;

R^1 and R^2 are attached to adjacent carbon atoms in Ar, and
either R^1 is C_1-C_{10}-alkylene and R^2 is hydrogen, C_1-C_{10}-alkyl, C_1-C_{10}-alkoxy or halogen
or R^1 and R^2 together with the carbon atoms in Ar to which they are attached denote a 5-, 6- or 7-membered cycloaliphatic ring;

R^a is a bond or C_1-C_{10}-alkylene optionally substituted by hydroxy, C_1-C_{10}-alkoxy, C_6-C_{10}-aryl or C_7-C_{14}-aralkyl; and

Y is C_1-C_{10}-alkyl, C_1-C_{10}-alkoxy, C_2-C_{10}-alkenyl or C_2-C_{10}-alkynyl optionally substituted by halo, cyano, hydroxy, C_1-C_{10}-alkyl, C_1-C_{10}-alkoxy or halo-C_1-C_{10}-alkyl;

C_3-C_{10}-cycloalkyl optionally fused to one or more benzene rings and optionally substituted by C_1-C_{10}-alkyl, C_1-C_{10}-alkoxy, C_3-C_{10}-cycloalkyl, C_7-C_{14}-aralkyl, C_7-C_{14}-aralkyloxy or C_6-C_{10}-aryl, where C_3-C_{10}-cycloalkyl, C_7-C_{14}-aralkyl, C_7-C_{14}-aralkyloxy or C_6-C_{10}-aryl are optionally substituted by halo, hydroxy, C_1-C_{10}-alkyl, C_1-C_{10}-alkoxy or halo-C_1-C_{10}-alkyl;

C_6-C_{10}-aryl optionally substituted by halo, hydroxy, C_1-C_{10}-alkyl, C_1-C_{10}-alkoxy, C_1-C_{10}-haloalkyl, phenoxy, C_1-C_{10}-alkylthio, C_6-C_{10}-aryl, 4- to 10- membered heterocyclic ring having at least one ring nitrogen, oxygen or sulphur atom, or by NR^bR^c where R^b and R^c are each independently C_1-C_{10}-alkyl optionally substituted by hydroxy, C_1-C_{10}-alkoxy or phenyl or R^b may additionally be hydrogen;

phenoxy optionally substituted by C_1-C_{10}-alkyl, C_1-C_{10}-alkoxy or by phenyl optionally substituted by C_1-C_{10}-alkyl or C_1-C_{10}-alkoxy;

a 4- to 10-membered heterocyclic ring having at least one ring nitrogen, oxygen or sulphur atom, said heterocyclic ring being optionally substituted by halo, C_1-C_{10}-alkyl, C_1-C_{10}-alkoxy, halo-C_1-C_{10}-alkyl, C_6-C_{10}-aryl, C_7-C_{14}-aralkyl, C_7-C_{14}-aralkyloxy, C_1-C_{10}-alkoxycarbonyl or a 4- to 10-membered heterocyclyl-C_1-C_{10}-alkyl;

$-NR^dR^e$ where R^d is hydrogen or C_1-C_{10}-alkyl and R^e is C_1-C_{10}-alkyl optionally substituted by hydroxy, or R^e is C_6-C_{10}-aryl optionally substituted by halo, or R^e is a 4- to 10-membered heterocyclic ring having at least one ring nitrogen, oxygen or sulphur atom which ring is optionally substituted by phenyl or halo-substituted phenyl or R^e is C_6-C_{10}-arylsulfonyl optionally substituted by C_1-C_{10}-alkylamino or di(C_1-C_{10}-alkyl)amino;

$-SR^f$ where R^f is C_6-C_{10}-aryl or C_7-C_{14}-aralkyl optionally substituted by halo, C_1-C_{10}-alkyl, C_1-C_{10}-alkoxy or C_1-C_{10}-haloalkyl; or

$-CONHR^g$ where R^g is C_1-C_{10}-alkyl, C_3-C_{10}-cycloalkyl or C_6-C_{10}-aryl; and

(B) a corticosteroid, for simultaneous, sequential or separate administration in the treatment of an inflammatory or obstructive airways disease, the molar ratio of (A) to (B) being from 100:1 to 1:300.

Claim 22 (new): A medicament according to claim 21, which is a pharmaceutical composition comprising a
mixture of effective amounts of (A) and (B) optionally together with at least one pharmaceutically acceptable carrier.

Claim 23 (new): A medicament according to claim 21, in which (A) is a compound of formula I in free or salt or solvate form wherein
X is $-R^1-Ar-R^2$ or $-R^a-Y$;
Ar denotes a phenylene group optionally substituted by halo, C_1-C_{10}-alkyl, C_1-C_{10}-alkoxy or by C_1-C_{10}-alkoxy substituted by phenyl;
R^1 and R^2 are attached to adjacent carbon atoms in Ar, and
either R^1 is C_1-C_{10}-alkylene and R^2 is hydrogen,
or R^1 and R^2 together with the carbon atoms in Ar to which they are attached denote a 5-, 6- or 7-membered cycloaliphatic ring;
R^a is a bond or C_1-C_{10}-alkylene optionally substituted by hydroxy, C_6-C_{10}-aryl or C_7-C_{14}-aralkyl; and
Y is C_1-C_{10}-alkyl, C_1-C_{10}-alkoxy or C_2-C_{10}-alkynyl; C_3-C_{10}-cycloalkyl optionally fused to one or more benzene rings and optionally substituted by C_1-C_{10}-alkyl, C_3-C_{10}-cycloalkyl, C_7-C_{14}-aralkyl, C_7-C_{14}-aralkyloxy optionally substituted by halo, or by C_6-C_{10}-aryl optionally substituted by C_1-C_{10}-alkyl or C_1-C_{10}-alkoxy; C_6-C_{10}-aryl optionally substituted by halo, hydroxy, C_1-C_{10}-alkyl, phenoxy, C_1-C_{10}-alkylthio, C_6-C_{10}-aryl, a 4- to 10-membered heterocyclic ring having at least one ring nitrogen atom, or by NR^bR^c where R^b and R^c are each independently C_1-C_{10}-alkyl optionally substituted by hydroxy or phenyl or R^b may additionally be hydrogen; phenoxy optionally substituted by C_1-C_{10}-alkoxy; a 4- to 10-membered heterocyclic ring having at least one ring nitrogen or oxygen atom, said heterocyclic ring being optionally substituted by C_1-C_{10}-alkyl, C_6-C_{10}-aryl, C_7-C_{14}-aralkyl, C_1-C_{10}-alkoxycarbonyl or by a 4- to 10-membered heterocyclyl-C_1-C_{10}-alkyl; $-NR^dR^e$ where R^d is hydrogen or C_1-C_{10}-alkyl and R^e is C_1-C_{10}-alkyl, or R^e is a 4- to 10-membered heterocyclic ring having at least one ring nitrogen or oxygen atom which ring is optionally substituted by halo-substituted phenyl or R^e is C_6-C_{10}-arylsulfonyl optionally substituted by di(C_1-C_{10}-alkyl)amino; $-SR^f$ where R^f is C_6-C_{10}-aryl or C_7-C_{14}-aralkyl optionally substituted by halo or C_1-C_{10}-haloalkyl; or $-CONHR^g$ where R^g is C_3-C_{10}-cycloalkyl or C_6-C_{10}-aryl.

Claim 24 (new): A medicament according to claim 23, in which (A) is a compound of formula I in free or salt or solvate form wherein

X is $-R^1-Ar-R^2$ or $-R^a-Y$;

Ar denotes a phenylene group optionally substituted by halo, C_1-C_4-alkyl, C_1-C_4-alkoxy or by C_1-C_4-alkoxy substituted by phenyl;

R^1 and R^2 are attached to adjacent carbon atoms in Ar, and

either R^1 is C_1-C_4-alkylene and R^2 is hydrogen,

or R^1 and R^2 together with the carbon atoms in Ar to which they are attached denote a 5-, 6- or 7-membered cycloaliphatic ring, especially a 5-membered cycloaliphatic ring;

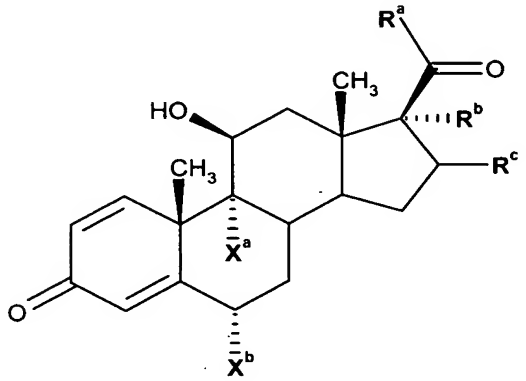
R^a is a bond or C_1-C_4-alkylene optionally substituted by hydroxy, C_6-C_8-aryl or C_7-C_{10}-aralkyl; and

Y is C_1-C_4-alkyl, C_1-C_4-alkoxy or C_2-C_4-alkynyl; C_3-C_6-cycloalkyl optionally fused to one or more benzene rings and optionally substituted by C_1-C_6-alkyl, C_3-C_6-cycloalkyl, C_7-C_{10}-aralkyl, C_7-C_{10}-aralkyloxy optionally substituted by halo, or by C_6-C_8-aryl optionally substituted by C_1-C_4-alkyl or C_1-C_4-alkoxy; C_6-C_8-aryl optionally substituted by halo, hydroxy, C_1-C_4-alkyl, phenoxy, C_1-C_4-alkylthio, C_6-C_8-aryl, a 4- to 8-membered heterocyclic ring having at least one ring nitrogen atom, or by NR^bR^c where R^b and R^c are each independently C_1-C_4-alkyl optionally substituted by hydroxy or phenyl or R^b may additionally be hydrogen; phenoxy optionally substituted by C_1-C_4-alkoxy; a 4- to 8-membered heterocyclic ring having at least one ring nitrogen or oxygen atom, said heterocyclic ring being optionally substituted by C_1-C_4-alkyl, C_6-C_8-aryl, C_7-C_{10}-aralkyl, C_1-C_4-alkoxycarbonyl or by a 4- to 8-membered heterocyclyl-C_1-C_4-alkyl; $-NR^dR^e$ where R^d is hydrogen or C_1-C_4-alkyl and R^e is C_1-C_4-alkyl, or R^e is a 4- to 8-membered heterocyclic ring having at least one ring nitrogen or sulphur atom which ring is optionally substituted by halo-substituted phenyl or R^e is C_6-C_8-arylsulfonyl optionally substituted by di(C_1-C_4-alkyl)amino; $-SR^f$ where R^f is C_6-C_8-aryl or C_7-C_{10}-aralkyl optionally substituted by halo or C_1-C_4-haloalkyl; or $-CONHR^g$ where R^g is C_3-C_6-cycloalkyl or C_6-C_8-aryl.

Claim 25 (new): A medicament according to claim 24, in which (A) is selected from the group consisting of 4-hydroxy-7-(1-hydroxy-2-{2-[4-(4-phenyl-butoxy)-phenyl]-ethylamino}-ethyl)-3H-benzothiazol-2-one; 7-[(R)-2-(1,1-dimethyl-2-phenyl-ethylamino)-1-hydroxy-ethyl]-4-hydroxy-3H-benzo-thiazol-2-one; 4-hydroxy-7-{(R)-1-hydroxy-2-[2-(5,6,7,8-tetrahydro-naphthalen-2-yl)-ethyl-amino]-ethyl}-3H-benzothiazol-2-one formate; 7-[(R)-2-((1S,2S)-2-benzyloxy-cyclopentyl-amino)-1-hydroxy-ethyl]-4-hydroxy-3H-benzo-thiazol-2-one; and 7-

[(R)-2-((1S,2R)-2-benzyloxy-cyclopentylamino)-1-hydroxy-ethyl]-4-hydroxy-3H-benzothiazol-2-one.

Claim 26 (new): A medicament according to claim 21, in which (B) is a compound of formula X



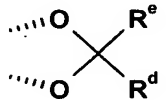
X

or a 1,2-dihydro derivative thereof, where

R^a is C_1-C_4-alkyl optionally substituted by halogen (preferably chlorine or fluorine), hydroxy, C_1-C_4-alkoxy, acyloxy or by C_1-C_4-acylthio, or R^a is C_1-C_4-alkoxy or C_1-C_4-alkylthio optionally substituted by halogen, or R^a is 5-or 6-membered heterocyclylthio, or R^a is C_1-C_4-alkylthio optionally substituted by halogen (preferably chlorine or fluorine),

either R^b is acyloxy and R^c is hydrogen or C_1-C_4-alkyl,

or R^b and R^c together denote a group of formula XI



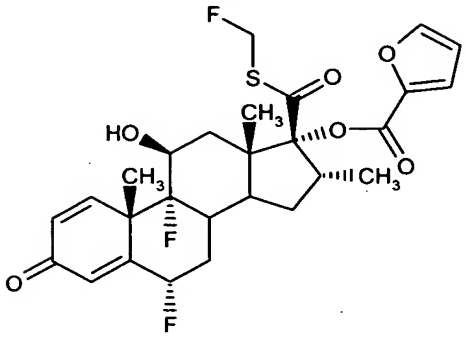
XI

where R^d is C_1-C_4-alkyl or C_3-C_6-cycloalkyl and R^e is hydrogen or C_1-C_4-alkyl,

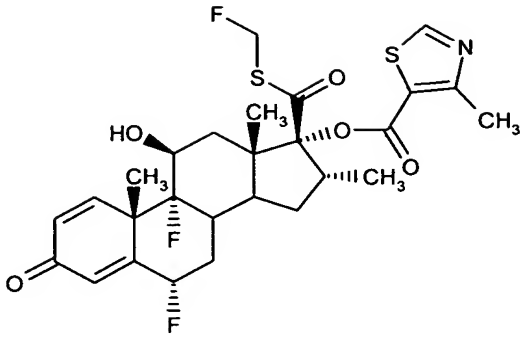
X^a and X^b are each independently hydrogen, chlorine or fluorine.

Claim 27 (new): A medicament according to claim 26, in which (B) is a compound selected from the group consisting of beclamethasone dipropionate, budesonide, fluticasone propionate, mometasone furoate, ciclesonide, triamcinolone acetonide, flunisolide, rofleponide

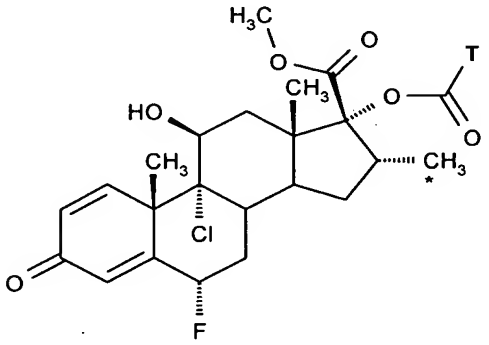
palmitate, butixocort propionate, icometasone enbutate,



and



Claim 28 (new): A medicament according to claim 26, in which (B) is a compound of formula XII



XII

where T is a monovalent cyclic organic group having from 3 to 15 atoms in the ring system.

Claim 29 (new): A medicament according to claim 28, in which T is a heterocyclic aromatic group having a 5-membered heterocyclic ring with one, two or three ring hetero atoms selected from nitrogen, oxygen and sulfur, the heterocyclic ring being unsubstituted or substituted by one or two substituents selected from halogen, C_1-C_4-alkyl, halo-C_1-C_4-alkyl, C_1-C_4-alkoxy, C_1-C_4-alkylthio, cyano or hydroxy-C_1-C_4-alkyl, and the heterocyclic ring being optionally fused to a benzene ring.

Claim 30 (new): A medicament according to claim 28, in which T is a heterocyclic aromatic group having a 6-membered heterocyclic ring with one or two ring nitrogen atoms, the heterocyclic ring being unsubstituted or substituted by one or two substituents selected from halogen, cyano, hydroxyl, C_1-C_4-acyloxy, amino, C_1-C_4 alkylamino, di-(C_1-C_4-alkyl)amino, C_1-C_4-alkyl, hydroxy-C_1-C_4-alkyl, halo-C_1-C_4-alkyl C_1-C_4-alkoxy, or C_1-C_4-alkylthio and the heterocyclic ring being optionally fused to a benzene ring.

Claim 31 (new): A medicament according to claim 28, where the indicated 16-methyl group has the alpha conformation and T is 5-methyl-2-thienyl, N-methyl-2-pyrrolyl, cyclopropyl, 2-furyl, 3-methyl-2-furyl, 3-methyl-2-thienyl, 5-methyl-3-isoxazolyl, 3,5-dimethyl-2-thienyl, 2,5-dimethyl-3-furyl, 4-methyl-2-furyl, 4-(dimethylamino)phenyl, 4-methylphenyl, 4-ethylphenyl, 2-pyridyl, 4-pyrimidyl or 5-methyl-2-pyrazinyl or the indicated 16-methyl group has the beta conformation and R is cyclopropyl.

Claim 32 (new): A medicament according to claim 21, wherein (A) is 7-[(R)-2-((1S,2S)-2-benzyloxy-cyclopentylamino)-1-hydroxy-ethyl]-4-hydroxy-3H-benzothiazol-2-one and (B) is budesonide, fluticasone propionate or mometasone furoate.

Claim 33 (new): A medicament according to claim 21, which is in inhalable form and is
(i) an aerosol comprising a mixture of (A) and (B) in solution or dispersion in a propellant; or
(ii) a combination of an aerosol containing (A) in solution or dispersion in a propellant with an aerosol containing (B) in solution or dispersion in a propellant; or
(iii) a nebulizable composition comprising a dispersion of (A) and (B) in an aqueous, organic or aqueous/organic medium; or
(iv) a combination of a dispersion of (A) in an aqueous, organic or aqueous/organic medium with a dispersion of (B) in an aqueous, organic or aqueous/organic medium.

Claim 34 (new): A medicament according to claim 21, in which (A) and/or (B) are present in inhalable form as a dry powder comprising finely divided (A) and/or (B) optionally together with at least one particulate pharmaceutically acceptable carrier.

Claim 35 (new): A medicament according to claim 34, in which (A) and/or (B) has an average particle diameter up to 10 μm.

Claim 36 (new): A medicament according to claim 21, in which the molar ratio of (A) to (B) is from 5:1 to 1:10.

Claim 37 (new): A medicament according to claim 22, which is
a dry powder in a capsule, the capsule containing a unit dose of (A), a unit dose of (B) and a pharmaceutically acceptable carrier in an amount to bring the total weight of dry powder per capsule to between 5 mg and 50 mg; or

a dry powder comprising, by weight, from 20-2000 parts of (A) in the form of the maleate salt, from 25-800 parts of (B) and 2000-25000 parts of a pharmaceutically acceptable carrier; or

an aerosol comprising (A) and (B) in a ratio as hereinbefore specified in claim 21, in a propellant, optionally together with a surfactant and/or a bulking agent and/or a co-solvent suitable for administration from a metered dose inhaler adapted to deliver an amount of aerosol containing a unit dose of (A) and a unit dose of (B), or a known fraction of a unit dose of (A) and a known fraction of a unit dose of (B), per actuation.

Claim 38 (new): A method of treating a subject suffering from an inflammatory or obstructive airways disease which comprises administering to that subject effective amounts of (A) and (B) as defined in claim 21.

Claim 39 (new): A method of treating a subject suffering from asthma or chronic obstructive pulmonary disease which comprises administering to that subject effective amounts of (A) and (B) as defined in claim 21.

Claim 40 (new): A pharmaceutical kit comprising (A) as defined in claim 21 and (B) as defined in claim 21 in separate unit dosage forms, said forms being suitable for administration of (A) and (B) in effective amounts, together with one or more inhalation devices for administration of (A) and (B).